Chronic Relapsing Pancreatitis

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SUMMARY

Chronic relapsing pancreatitis is a disease of recurring acute episodes of severe upper abdominal pain which are progressive and gradually may become so severe and so frequent as to be intractable.

Early in the disease the function of the gland and of the islet tissue may be disturbed only at the time of the acute attack, but subsequently these changes may become permanent and manifested by steatorrhea, creatorrhea and diabetes mellitus. The results of studies of pancreatic function parallel those of the pathologic process, and calcification of the pancreas is common.

Medical treatment is generally disappointing. Paravertebral injections may control acute pain. Surgical therapy is none too satisfactory. Long continued biliary drainage, anastomosis between the common bile duct and duodenum and between the pancreatic duct and duodenum, section of the sphincter of Oddi, partial and total pancreatectomy and sympathectomy, splanchnicectomy and vagotomy have been helpful in relieving pain and in preventing the recurrence of attacks in some instances.

MUCH interest in acute and chronic inflammatory diseases of the pancreas has been aroused in recent years, owing largely to excellent clinical and pathological descriptions by Comfort and his associates, and to increasing experience of various surgeons with partial and total pancreatectomy and with injections of or resections of nerves in the control of the painful seizures of these diseases. Diseases of the pancreas, with the exception of those manifested by diabetes mellitus or by advanced carcinomatous changes, have generally been difficult to diagnose clinically because of the inaccessible anatomic location of the organ and of the lack of satisfactory simple tests of pancreatic function.

Various apparently unrelated forms of acute and chronic pancreatitis have been described over a period of many years, but a clear-cut clinical concept of an entity now frequently called "chronic relapsing pancreatitis" was not developed until Comfort, Gambill and Baggenstoss in 1946 presented their studies of 27 such cases. They pointed out that this disease manifests itself by recurring attacks of pain, usually in the upper part of the abdomen, by disturbances of function of acinar and islet cells, and by certain sequelae.

Chronic relapsing pancreatitis is not a common disease (approximately 20 cases were encountered each year in the early 1940's at the Mayo Clinic) but it is now more frequently recognized than it was formerly. Curiously, it predominates in the male (6:1), and patients who have the disease are usually not obese. In these last two respects it differs from disease of the biliary tract. It is more common in patients in middle age (median 37 years) and in alcoholics.

ETIOLOGY AND PATHOLOGY

The cause of chronic relapsing pancreatitis is not clear and there has been wide discussion of the relation of it to disease of the gallbladder, bile ducts, and liver. Recent studies of Gambill, Comfort and Baggenstoss have indicated that the clinical picture, pathologic physiology, the course of the disease and the pathologic alterations in the pancreas in cases of chronic relapsing pancreatitis are very constant, regardless of the presence or absence of disease of the biliary tract. These findings, as well as the differences between the two diseases with regard to sex incidence and the presence of obesity, strongly suggest that pancreatitis is not necessarily secondary to disease of the biliary tract but may be and frequently is independent of it.

Baggenstoss has shown that grossly the pancreas, in cases of chronic relapsing pancreatitis, is indurated and sometimes nodular, and that, microscopically, fibroblastic proliferation and fibrosis are prominent features. Gross atrophy of the gland, pseudocyst formation and macroscopic calcification are characteristic of the disease. Interstitial fibrosis and residual necrosis of tissue are other constant findings. Fibrosis is usually interlobular, although intralobular and intra-acinar fibrosis occur. Infiltration with lymphocytes and plasma cells is common, but actual suppuration is rare. Insofar as associated changes in the bile ducts are concerned, it appears that this form of pancreatitis may be responsible for dilation of the gallbladder, and that the degree of pathologic change in the gallbladder and ducts bears some relationship to the extensiveness and activity of the disease in the pancreas.

SYMPTOMS

Recurring, acute, severe, prolonged exacerbations of upper abdominal pain, separated by intervals of

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relative or complete clinical quiescence, are characteristic of the disease. Pain is the outstanding clinical feature of the acute attack. The pain may begin gradually or suddenly, is generally in the upper abdomen, is severe, is prolonged (from several hours to several days), is variable in type but usually steady, and frequently and characteristically it radiates to the left upper quadrant of the abdomen and to the back. Often, repeated doses of opiates are needed for relief, and not infrequently the patients become addicted to opiates. The interval between attacks varies greatly; it may be years in the early stages of the disease. Usually as the disease progresses the intervals shorten and become marked by persisting digestive symptoms, signs of disturbance in pancreatic function, and at times by diabetes mellitus. In short, the disease tends to be progressive, the attacks becoming more frequent, more prolonged and more severe.

Accompanying the pain are variable symptoms of gastrointestinal dysfunction such as nausea, vomiting, constipation or diarrhea, abdominal distention, jaundice, bleeding and such general symptoms as weakness, fever, sweating and shock.

In the interval between attacks there are frequently no symptoms in the early stages of the disease. Later on, various non-specific clinical syndromes may develop with symptoms including intolerance to fatty foods, flatulence, weakness, constipation, anorexia and epigastric distress.

In approximately half of the cases observed by Comfort, Baggenstoss and Gambill, pronounced permanent sequelae including diabetes, steatorrhea and calcification of the pancreas were present and observable in the interval between acute painful exacerbations of the disease.

DIAGNOSIS

The diagnosis of chronic relapsing pancreatitis may be simple in a typical case when all of the characteristic features are present. On the other hand it may be extremely difficult in the patient whose only manifestation of the disease has been recurring attacks of upper abdominal pain.

The most useful diagnostic feature in the history is that of recurring, severe, protracted upper abdominal pain with features previously noted. Associated symptoms excepting jaundice are usually non-specific and in keeping with any severe abdominal pain due to an acute inflammatory process. Addiction to opiates may be present.

Physical examination during an attack may reveal moderate fever, epigastric tenderness and rigidity and jaundice. "The appearance of a rounded cystic mass in the pancreatic region during the painful seizure or soon thereafter may have the same significance as does diabetes mellitus, steatorrhea or calcification." (Gambill and co-workers.) In the interval between attacks examination may disclose no abnormality except for evidence of weight loss and epigastric tenderness.

Laboratory data obtained during an acute attack may reveal leukocytosis, acceleration of the sedimentation rate and evidence of jaundice. Glycosuria and transient hyperglycemia are infrequent unless diabetes mellitus is present. The following phenomena, if present, are useful in substantiating the diagnosis: Elevation of values for amylase and lipase in the serum and of the value for fecal solids, fat and nitrogen in the stool by chemical analysis, grossly fatty stools and excessive amounts of fat by microscopic examination. Even during an acute attack, however, results of tests mentioned may be within normal limits. In some cases in which accurate studies can be made of the volume and of the bicarbonate and enzymatic concentration of duodenal content after stimulation with secretin, the finding of values lower than normal may be useful to substantiate the diagnosis. Negative results of tests do not exclude the disease.

Roentgenologic studies are useful in ruling out other causes of severe abdominal pain in the stomach, duodenum, colon and gallbladder. They may also reveal multiple areas of calcification throughout the pancreas and, in fact, the gland may appear largely calcified. Abnormalities in the appearance of, or in the peristaltic activity of the stomach or duodenum in those areas where they are contiguous with the pancreas, may be a useful confirmatory diagnostic help in an occasional case.

Finally, the course followed by the patient may be diagnostically important because it may be typical —recurring acute, severe, prolonged, upper abdominal pain associated with transient elevations in value of serum lipase or amylase, and perhaps hyperglycemia and glycosuria during the attack, generally followed over a period of years by more severe and more prolonged attacks of pain, by prominent physiological alterations in glucose metabolism and by development of steatorrhea and creatorrhea. Such a pattern generally establishes the diagnosis. If in addition radiological evidence of calcification of the pancreas is found, the diagnosis is clear.

In many patients with this disease the diagnosis is not established until operation is performed. In fact, in over half the cases the correct diagnosis is not made preoperatively. It is particularly liable to be missed in those cases in which symptoms resemble those of biliary tract disease — namely, jaundice and colics—and there is no laboratory evidence of pancreatic disease.

TREATMENT

Treatment of the attack of acute pancreatitis is generally considered a medical problem, whereas surgical treatment may be advisable and helpful in managing the patient with recurring attacks of pain or with associated disease in the biliary tract.

Medical: Medical treatment of the acute attack is largely symptomatic and consists of administration of ephedrine sulfate, papaverine hydrochloride or opiates, and of intravenous administration of fluids, of decompression of the upper gastrointestinal tract and control of shock if these measures are necessary.

Between episodes and when the disease becomes chronic, medical treatment consists of high caloric, high carbohydrate, low fat diet, control of diabetes if it is present, and avoidance of alcohol. Extract of the whole pancreas in doses of 5 gm. in enteric-coated tablets with each meal may help greatly in reducing abdominal discomfort and increasing absorption of food.

Surgical: In discussion of surgical treatment of chronic relapsing pancreatitis, consideration must be given to the end to be accomplished. The principal problem may be any of the following: To relieve the acute attack of pain, to attempt to prevent recurrence of severe attacks of pain, to improve pancreatic function, to relieve accompanying jaundice, or to remove associated disease of the biliary tract.

For the control of pain in the immediate attack, paravertebral block, with novocain, of the sixth to tenth dorsal segments has been advocated by deTakats and Walter, White and Smithwick, and others. Properly carried out, this method appears to be very effective, although it may have to be repeated several times during an acute episode. While this method of treatment would appear largely to control pain only and not to influence the disease process in the pancreas, some advocates of it believe that because spasm of the sphincter of Oddi may be relieved, promoting drainage from the pancreas, the method may actually affect the pathologic process.

Other more time-honored surgical methods of control of acute attacks, as well as of the lesion, include cholecystostomy with prolonged drainage and cholecystectomy with prolonged (six to 12 months) drainage of the common bile duct by a T-tube. It must be readily appreciated, however, that when drainage of the biliary tract is discontinued the pathologic process of the pancreas may progress and symptoms reappear.

Surgical procedures which have been recommended to control recurrent attacks of pain and to improve pancreatic function, and which are therefore most useful in the earlier stages of the disease, include choledochoduodenostomy, which has been particularly advocated by Waugh, and section of the sphincter of Oddi. The latter method, which has recently been applied in 21 cases by Doubilet and Mulholland, is carried out by an approach through the common duct or by opening the duodenum and directly sectioning the muscle over a probe. The rationale of this procedure goes back to the original suggestion of Archibald, that spasm of the sphincter of Oddi in the presence of a common biliary-pancreatic passageway and reflux of bile into the pancreas is a significant etiologic factor in acute pancreatitis.

Two other surgical procedures advocated for the disease include anastomosis of the dilated pancreatic duct to the duodenum, as reported by Crile, and ligation of the pancreatic duct, which according to Martin and Canesco is a treatment of choice at the Johns Hopkins Hospital Clinic. Crile states that the anastomotic procedure has given relief to approximately 50 per cent of patients operated upon and is therefore not a specific cure. The other procedure, ligation of the duct, leads to atrophy of the pancreatic acini without accompanying atrophy of the islands of Langerhans.

Finally, for those patients with extensive disease of the pancreas, manifested chiefly by recurring, severe, almost uncontrollable pain, the two most commonly advocated procedures include partial or total pancreatectomy and section of the sympathetic and/or parasympathetic nerve fiber supplying the pancreatic area. Whipple recently (1946) collected reports of 12 cases of total pancreatectomy from the literature and added two of his own. While this a heroic procedure with a great morbidity and high mortality rate, it would appear to be justified in an occasional patient with intractable pain who is perhaps already diabetic. Before carrying out such an extensive procedure, consideration should be given to a less serious operation such as section of nerves. Crile, deTakats and Walter, and others, have advocated ganglionectomy on the right side (seventh to twelfth dorsal) with or without resection of the right splanchnic nerve. While Rienhoff and Baker have reported section of both splanchnic nerves and both vagi with striking relief of pain, there is question whether in all cases such an extensive surgical procedure is necessary.

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